Nivolumab improves the proportion of lung cancer patients alive after more than a year

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Patients with a type of lung cancer called non-squamous non-small cell lung cancer (non-SQ NSCLC) have limited treatment options and a dismal prognosis once their disease has advanced and initial treatment with platinum-based chemotherapy has failed. Second-line treatment is usually with another chemotherapy drug, such as docetaxel or pemetrexed.

Recent results have shown that the drug, nivolumab, improves survival for these patients and now updated results from the CheckMate 057 phase III clinical trial, to be reported at the 2015 European Cancer Congress today (Monday) with simultaneous publication of the study results in the *New England Journal of Medicine*, show that nivolumab continues to show an overall survival benefit compared to docetaxel. Among patients randomised to receive nivolumab, significantly more were alive at 12 months compared to those treated with docetaxel - 51% versus 39% respectively - and a difference in survival remains at 18 months - 39% for nivolumab versus 23% for docetaxel.

This improvement in survival was observed for all patients included in the trial, but nivolumab was more effective in patients whose tumours expressed a protein called programmed death ligand 1 (PD-L1), which plays a role in the immune system's ability to recognise and attack tumours and has been correlated with response to immune checkpoint inhibitors such as nivolumab.

The researchers found there was a difference in the objective response

rate (ORR) between patients with tumours expressing different levels of PD-L1 (ORR is the proportion of patients who experience a reduction in tumour size for a minimum time period). However, PD-L1 made little difference to the duration of the response in the patients on nivolumab. There was an ORR of 31% among patients with tumours expressing PD-L1 in at least one percent of cells, compared to nine percent in patients with tumours with PD-L1 expressed in less than one percent of cells. However, the difference in the median duration of the response was 16 months versus 18.3 months respectively, which was not statistically significant. Among patients receiving docetaxel the duration of response was 5.6 months, regardless of PD-L1 expression.

Leora Horn, Associate Professor of Medicine at the Vanderbilt Ingram Cancer Center, Nashville, USA, will tell the Congress: "The results from this trial show that for patients with non-squamous non-small cell lung cancer who have progressed on prior platinum-based chemotherapy, nivolumab is a good treatment option showing durable benefit with fewer side effects regardless of PD-L1 tests results compared to treatment with docetaxel."

Patients treated with nivolumab suffered fewer significant treatment-related adverse events (grades 3-4) compared to patients on docetaxel: 10% and 54% respectively. Data presented at the Congress show that this was regardless of PD-L1 expression. There were 13% and 53% treatment-related grade 3-4 side effects for nivolumab and docetaxel respectively in patients with tumours that stained positive for PD-L1 in at least one percent of cells, compared to 8% and 58% for nivolumab and docetaxel respectively in patients with tumours that stained positive for PD-L1 in less than one percent of cells. Moreover, patient-reported outcomes, as measured by the Lung Cancer Symptom Scale, showed a better quality of life with slower deterioration for patients treated with nivolumab compared to docetaxel.

In the international clinical trial, 292 patients were randomised to receive treatment with nivolumab at a dose of 3 mg/kg administered intravenously every two weeks and 290 received docetaxel at a dose of 75 mg/m2 intravenously every three weeks. Treatment continued until the cancer progressed or patients discontinued due to toxic side effects.

"Similar to prior studies, response rates to nivolumab were higher in current and former smokers compared to never smokers: 22% and 9% compared to 11% and 15% for docetaxel respectively. Responses were observed in patients with and without cancer-driving mutations in the epidermal growth factor receptor (EGFR): 11% and 18% respectively with nivolumab compared to 16% and 9% respectively with docetaxel," said Professor Horn.

Professor Peter Naredi, the ECCO scientific co-chair of the Congress, who was not involved in the research, commented: "At the European Cancer Congress this year we are fortunate to have many presentations of randomised phase III trials that will most likely change the stage for treatment of cancer. Professor Horn and a group of collaborators in Europe and the US now show that nivolumab, a PD-1 immune checkpoint inhibitor, is also effective in non-squamous non-small cell lung cancer. This will be important for all those patients for whom prior treatment with chemotherapy has failed."

More information: "Nivolumab versus docetaxel in advanced non-squamous non-small cell lung cancer", by Hossein Borghaei et al. DOI: 10.1056/NEJMoa1507643 . Published online: www.nejm.org/doi/full/10.1056/NEJMoa1507643

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